Supervised Graph Inference

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Motivations: systems biology

- Gene expression
- Sequence
- Protein structure
- Protein localization, etc...
- Regulatory network
- Signaling pathways
- Metabolic pathways
- Interaction network, etc...
Related approaches

- Bayesian nets for regulatory networks (Friedman et al. 2000)
- Boolean networks (Akutsu, 2000)
- Nearest neighbors method (Marcotte et al., 1999)
Example: nearest neighbors method
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**Application: metabolic network reconstruction**

The **metabolic network** of the yeast involves **769 genes**. Each gene is represented by **157 expression measurements**. (ROC=0.52)
What is wrong?

- What similarity measure between profiles should be used?
What is wrong?

- What similarity measure between profiles should be use?
- Which network are we expecting to recover?
The supervised gene inference problem
The supervised gene inference problem
The main idea

Supervised graph inference through distance metric learning
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through
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Learning the mapping $\Phi$

- Let us consider mappings $\mathcal{X} \to \mathbb{R}^d$ ($\mathcal{X}$ being endowed with a p.d. kernel $K$):
  \[
  \Phi(x) = (f_1(x), \ldots, f_d(x))' \in \mathbb{R}^d
  \]
  made of orthogonal features $f_i \in \mathcal{H}_K$ in the RKHS
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- A possible criterion to ensure that connected genes in the known network have similar value is to minimize:

$$\min_{f \in \mathcal{H}_K} \frac{\sum_{(i,j) \in E} (f(x_i) - f(x_j))^2 - \sum_{(i,j) \notin E} (f(x_i) - f(x_j))^2}{\sum_{i=1}^n f(x_i)^2}$$
Regularized risk

- If the data are centered ($\sum_i x_i = 0$), then this is equivalent to minimizing:

$$\min_{f \in \mathcal{H}_K} \frac{\sum_{i \sim j} (f(x_i) - f(x_j))^2}{\sum_{i=1}^n f(x_i)^2}.$$
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- For statistical reasons (particularly in large dimension), it is safer to minimize:

$$\min_{f \in \mathcal{H}_K} \frac{\sum_{i \sim j} (f(x_i) - f(x_j))^2 + \lambda ||f||^2}{\sum_{i=1}^n f(x_i)^2}.$$
Influence of $\lambda$

- $\lambda \to +\infty$: kernel PCA
  - Useful for noisy, high-dimensional data.
  - Used in spectral clustering. The graph does not play any role (unsupervised)

- $\lambda \to 0$: second smallest eigenvector of the graph
  - Useful to embed the graph in a Euclidean space (used in graph partitioning)
  - Sensitive to noise. Mapping of points outside of the graph unstable (overfitting)
Extracting successive features

- Successive features to form $\Phi$ can be obtained by:

$$f_i = \arg\min_{f \perp \{f_1, \ldots, f_{i-1}\}} \left\{ \frac{\sum_{i \sim j} (f(x_i) - f(x_j))^2 + \lambda \|f\|^2}{\sum_{i=1}^{n} f(x_i)^2} \right\}.$$
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• The solution satisfies $f_i(x) = \sum_j \alpha_{i,j} K(x_j, x)$, where $\alpha_i$ are the successive generalized eigenvectors of

$$(LK_V + \lambda I) \alpha = \mu K_V \alpha.$$
Evaluation of the supervised approach: effect of $\lambda$

Metabolic network, 10-fold cross-validation, 1 feature
Evaluation of the supervised approach: number of features ($\lambda = 2$)
Learning from heterogeneous data

- Suppose several data are available about the genes, e.g., expression, localization, structure, predicted interaction etc...

- Each data can be represented by a positive definite similarity matrix $K_1, \ldots, K_p$ called kernels

- Kernel can be combined by various operations, e.g., addition:

\[ K = \sum_{i=1}^{p} K_i \]
Learning from heterogeneous data (unsupervised)
Learning from heterogeneous data (supervised)
Conclusion
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2. Supervised graph inference can be performed by **distance metric learning**
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2. Supervised graph inference can be performed by **distance metric learning**

3. **Data integration with kernels** is simple and powerful

See you at **poster 49**